

March 17, 1999

1070 '99 MAR 23 A9 57

Dockets Management Branch (HFA-305)  
Food and drug Administration  
Room 1061  
5630 Fishers Lane  
Rockville, MD 20852

Re: Docket No. 98D-1165  
Draft Guidance for the Content of Premarket Notifications [510(k)s] for Electrocor-  
poreal Shock Wave Lithotripters Indicated for the Fragmentation of Kidney and  
Ureteral Calculi

Dear Sir/Madam:

On behalf of a holder of an approved premarket approval application (PMA) for an electrocor-  
poreal shock wave lithotripter (ESWL), I am submitting the enclosed comments on the above  
referenced draft guidance. My client is supportive of the FDA proposed rule to reclassify  
ESWL devices into Class II. On their behalf I will be submitting comments on the proposed  
rule under separate cover. Our enclosed comments on the draft guidance will address the  
provisions in the same order as they appear in the document. We conclude our comments by  
addressing an issue not specifically covered in the draft guidance, i.e., the regulation of  
replacement ESWL shock plugs.

Page 3: Predicate Device

Section 216 of the FDA Modernization Act of 1997 (FDAMA) amended section 520(h)(4) of  
the Federal Food, Drug, and Cosmetic Act (the Act) to make available safety and effective-  
ness information in an approved PMA for FDA use, among other things, in approving or  
reclassifying another device 6 years after FDA approval of the PMA. The publicly available  
summaries of safety and effectiveness information required by section 520(h)(1)(A) of the Act  
are thereby available to FDA as the evidentiary basis for FDA approval or reclassification of  
another device.

In light of this FDAMA provision, FDA should revise the draft guidance to require 510(k)  
applicants to demonstrate that the cited predicate device is legally marketed under either a  
FDA cleared 510(k) submission or an original PMA/PMA supplement approved at least 6  
years prior to the submission of the applicant's 510(k).

Citation of a modified version marketed under an approved PMA supplement, however, may not be possible as a publicly available summary of the safety and effectiveness data does not presently exist for ESWL models or modifications marketed via PMA supplement approval. Until at least one firm has obtained 510(k) clearance for such a modified device, a competitor's predicate device cited by a 510(k) applicant should be limited to that in the competitor's original PMA. The 510(k) applicant should then be required to address the differences in technological characteristics as prescribed in an applicable FDA law, regulation and guidance to demonstrate that no new issues of safety or effectiveness exist and its device is as safe and effective as the cited predicate device. FDA needs to address this PMA supplement issue if it proceeds to finalize this reclassification of ESWLs..

As an aid to 510(k) applicants in identifying appropriate predicate devices, FDA should include in the guidance a revision of the chronological listing of PMA/PMA supplement approvals currently available through the CDRH web site. Revisions of most listings are needed to identify the device model number(s) or modification(s) covered by the PMA/PMA supplement approval.

#### Page 4: Intended Use

The suggested indication for use in the draft guidance is inconsistent with that in PMA/PMA supplement approvals for ESWLs to date. In the latter case FDA has in certain cases placed limitations on the size range of the urinary stones to be fragmented and the region of the ureter to be treated. This usually occurs when there is an insufficient number of appropriate patients enrolled in the clinical study to support a broader indication for use. No such limitations appear in the intended use suggested in the draft guidance. It appears that the 510(k) applicant can label its ESWL for use in fragmenting all size stones and those in the upper, middle, lower or entire ureter without FDA requiring sufficient valid scientific evidence to support this broad intended use. If FDA proceeds with the reclassification, the final guidance and final classification rule need to clarify this issue and, if appropriate, indicate what holders of approved PMAs must do to remove any existing limitations in the indications for use of their ESWL.

#### Page 8: Clinical Performance Testing

The suggested confirmatory clinical study for demonstrating substantial equivalence would permit as few as 20 patients to be enrolled at two investigational sites with only a follow-up at 1-week post-procedure. The guidance is unclear whether there should be at least 20 patients at each of two sites or a total of 20 patients between two sites. Either way, a clinical study of such low magnitude does not lend itself to any meaningful statistical evaluation. On a random selection basis, it would not be expected to enroll patients representative of the patient population in the indication for use suggested in this draft guidance and discussed in the preceding paragraph. If the final guidance continues to provide for confirmatory clinical studies of this low magnitude, it should justify the adequacy of such studies in demonstrating substantial equivalence. This is especially necessary as neither the draft guidance nor the proposed reclassification rule cite postmarket surveillance as one of the special controls deemed necessary to demonstrate in a 510(k) submission that a new or modified ESWL is as safe and effective as the cited predicate device(s).

For a new or significantly modified ESWL with an operating principle and shock wave characteristics similar to the cited predicate device(s), a confirmatory clinical study for demonstrating substantial equivalence should involve at least 3 investigational sites, a minimum of 30 patients per site, and the assessment of treatment success and adverse effects immediately post-procedure and at 2-weeks and 1-month thereafter. This study lends itself to a meaningful statistical evaluation and should allow for a study population representative of the intended use. It should also permit the 510(k) applicant and FDA to determine whether the success rate is consistent with marketed ESWLs and whether its adverse event experience is consistent with the standardized adverse event information to be required in the labeling.

We support the provision on page 9 of the draft guidance that the addition of device-specific claims regarding the clinical performance of the applicant's ESWL must be demonstrated by sufficient clinical data to statistically support the claim. The draft guidance should be revised to clearly indicate that such a claim requires FDA clearance of a 510(k) before it can be included in the firm's labeling, advertisements, and other promotional materials for its device. We are concerned, however, that FDA apparently lacks the authority to revoke 510(k) clearances and may grant 510(k) clearances for comparative performance claims based upon erroneous or unsupportable information. The confirmatory clinical studies suggested in the draft guidance will not provide a study population comparable to those in approved PMAs and cannot support claims of superior safety and effectiveness. We suggest that the guidance clearly indicate that FDA will not accept 510(k) submissions for comparative performance claims as such claims are inappropriate for 510(k) review and, in all likelihood, unsupportable for substantially equivalent devices. The guidance should identify the types of clinical performance claims that are appropriate for 510(k) review and clearance.

#### Page 9: Labeling

The guidance inappropriately cites section 515(d)(1)(B)(ii) of the Act as the authority for restricting the device to physicians trained and/or experienced in the use of the device as outlined in the required training program. This is the statutory authority that applies to PMA approval orders only and is cited in the PMA approval orders for ESWLs and most other PMA approved devices. In addition to restricting the use of the PMA approved device, it implements the FDA authority to regulate its advertising. FDA is required to go through a rulemaking process in order to designate other devices as restricted devices. The proposed reclassification rule published in the February 8, 1999 *Federal Register* appropriately cites section 520(e) of the Act as the authority to restrict the use of the reclassified ESWLs.

Because ESWLs are presently, and will continue to be, restricted devices and not simply prescription devices under 21 CFR 801.109, the restricted device legend should be revised to read:

“CAUTION: Federal law restricts this device to sale, distribution, and use only upon the lawful order of a physician trained and/or experienced in the use of this device as outlined in the required training program.”

The legend on pages 9 and 19 (Appendix 2: SWL Labeling Template) in the draft guidance is consistent with 21 CFR 801.109 but only restricts the sale, and not the distribution and use, of the device. This suggested revision more appropriately conforms to the provisions in section 520(e) of the Act for restricted devices.

Pages 12 and 13 of the draft guidance provide for standardized information regarding the expected frequency of potential adverse events. The guidance needs to clarify whether a firm can continue to include in its labeling the adverse event data from the clinical studies supporting its PMA approval in lieu of the standardized information. We suggest that the PMA holder be given an option in this matter. FDA approval of a PMA is based upon a determination that the PMA includes sufficient valid scientific evidence to provide reasonable assurance of the device's safety and effectiveness for its intended use. Use of the standardized adverse event information is appropriate, and should be required, when the clinical study data in the applicant's 510(k) does not meet the PMA approval criteria for providing reasonable assurance of safety and effectiveness or does not build upon the safety and effectiveness information contained in an approved PMA held by the same applicant.

#### Page 14: Training Program

The restricted device legend required in the device labeling clearly indicates that the required physician training must extend beyond simply providing each physician, who intends to use the firm's ESWL, with training materials such as a User's Manual or a videotape demonstrating the use of the device. FDA apparently intends that there be some form of documented hands-on training or appropriately supervised use of the device.

Lack of consistency in the physician training programs cleared via 510(k)s could create significant product liability and litigation issues for manufacturers and physicians. The final guidance should include information needed to provide this consistency. Because of the 15-year experience with the use of ESWLs in the United States, FDA should not require in all cases that the hands-on training or supervision be provided by a trained representative of the manufacturer. Training by a physician already trained and experienced in the use of the manufacturer's ESWL should suffice. FDA should offer suggestions as to how this training is to be documented and how the documentation is to be maintained.

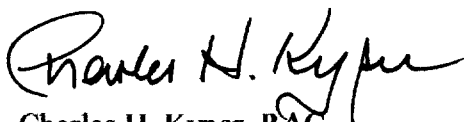
#### Regulation of Replacement ESWL Shock Plugs

On September 6, 1990, FDA approved a PMA (P870011) for an ESWL shock plug as a replacement component for a specific model of a competitor's ESWL. PMA supplement approval with supporting clinical studies beyond those suggested in the draft guidance is required each time the manufacturer develops a replacement shock plug for an additional ESWL model. Under section 216 of FDAMA the safety and effectiveness information in this PMA is now available for FDA use to allow firms to market replacement shock plugs for any and all marketed ESWLs via the 510(k) process.

The proposed reclassification rule and draft ESWL guidance, however, do not indicate whether the proposed reclassification applies to replacement ESWL shock plugs when manufactured and distributed by a firm other than the manufacturer of the ESWL. FDA needs to clarify this matter in both the final reclassification rule and the associated guidance. The guidance may need to have a specific section addressing the 510(k) content requirements for firms that manufacture and market replacement shock plugs for ESWLs other than their own. The draft ESWL guidance directs the reader to another FDA document for guidance when additional 510(k) clearance is needed for a modification of a marketed device. Because this latter guidance is not device-specific and lends itself to varying interpretations, we suggest that the final ESWL guidance require these firms to obtain 510(k) clearance when they propose to market a replacement shock plug for an additional model of a another firm's marketed ESWL. Each 510(k) clearance should be supported by a clinical study of sufficient magnitude to demonstrate that the clinical performance of the replacement shock plug is comparable to that of the shock plug supplied by the ESWL manufacturer.

We hope that the enclosed comments are helpful. Please do not hesitate to contact me if additional information or clarification is needed.

Sincerely,

A handwritten signature in black ink, appearing to read "Charles H. Kyper". The signature is fluid and cursive, with the first name "Charles" and last name "Kyper" clearly distinguishable.

Charles H. Kyper, RAC  
President

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